operation which is quite as easily justified as any of the major operations of surgery.

II. That so far as its secondary results are yet known, it is an operation which yields abundant encouragement for its further trial.

As conclusions which are indicated, but not wholly proved, I think I may formulate a statement that removal of the ovaries alone is not sufficient to arrest menstruation, but that removal of both tubes and ovaries does at once arrest it. So far as some of these cases have gone the arrest would seem to be permanent. This conclusion is quite in harmony with what is known of removal of both ovaries for large cystomata, for in such cases the tubes are almost uniformly included in the clamp or ligature, and menstruation is arrested.

Three at least of the cases, and probably two others, show that the arrest of menstruation by this means leads, or may lead, to the atrophy of the tumours.

Finally, there is some close connection, here pointed out I believe for the first time, and worthy of very clear study, between uterine myoma and its accompanying hemorrhages, and cystic disease of the ovaries. In two of the cases the cystic disease seemed to be the cause of the hemorrhage, without any myoma intervening.

Another conclusion is, I think, to be justified, that the whole subject is worthy of careful study, and should not be made the subject of premature and hostile conclusions.

ARTICLE III.

AN EXPERIMENTAL STUDY ON THE ACTION OF SALICYLIC ACID UPON BLOOD-CELLS AND UPON AMŒBOID MOVEMENTS AND EMIGRATION.

By T. MITCHELL PRUDDEN, M.D., Director of the Physiological and Pathological Laboratory of the Alumni Association of the College of Physicians and Surgeons, N. Y.; Lecturer on Normal Histology in Yale College; Pathologist to the Manhattan Eye and Ear Hospital.

IT was shown by the writer in a recent number of this JOURNAL, January 1881 (p. 82), that dilute carbolic acid possesses an inhibitory power over the amœboid movements and the capacity for emigration of the white blood-cells: and it was suggested as extremely probable, therefore, that a part of the favourable action of carbolic acid in the healing of wounds, at least in so far as the prevention of undue suppuration is concerned, is owing to the reduced activity of the white blood-cells. In view of this suggestive probability, for absolute proof is scarcely to be expected with our present facilities for investigation, it is evidently important to know whether the effects of other agents which exert a like favourable influence upon the healing process, can be partially or entirely accounted for on the same grounds. As one of the most important competitors for favour in antiseptic surgery salicylic acid is the first to suggest itself, and the purpose of the present article is to record a series of experiments with this agent similar to those just referred to with carbolic acid.

The methods used were essentially the same as those described in detail in the above-mentioned paper, and it will be necessary only to refer to them here, detaining the reader with little else than a brief account of the results. The experiments were largely made upon spring frogs of the species Rana clamitans,[1] but control experiments were made upon the blood of the rabbit and of man. The salicylic acid was dissolved in a half per cent. solution of sodium chloride, for the purpose of eliminating from the experiments, as much as might be, the action of water, by giving to the solutions a proper degree of concentration. It was used in solutions of the strength of 1–300; 1–500; 1–1000; 1–3000; 1–4000; 1–5000.

The first series of experiments upon frog's blood was made by irrigating, on a slide, the blood or mixed blood and lymph drawn from the toe.

Strong Solutions in Frog's Blood.—The effect of solutions of 1–500 and stronger, on both red and white blood-cells, is to cause rapid death of the cells and profound changes in the protoplasm. If such solutions are added to specimens in which the leucocytes are in active motion, as soon as it fairly comes in contact with them, all movement ceases at once, the cell processes are usually somewhat contracted and the cell body becomes more coarsely granular. The nucleus very soon becomes visible, then shrinks considerably, and presently the cell bodies appear to be broken up into larger and smaller irregular particles of strongly refractive material lying in a transparent matrix: the nuclei also undergo the same degeneration. After this no change occurs in the cells while they remain in the acid. Almost at the same instant that alterations are seen in the leucocytes changes commence in the red blood-cells. The first change observed is the rapidly increasing distinctness in the outline of the nucleus and of the intra-nuclear network, and sometimes hand in hand with this appears a slight irregularity in the contour of the cell. The observer must now be on the alert, for, sometimes almost faster than he can follow them, very marked changes occur in the cell body. At first an almost indefinable darkening of the body occurs, as if it were being suddenly shaded from the light below, this very rapidly deepens and merges into a mottling of the surface which usually, almost before it is defined, gives place to a distinct, shining, closemeshed, reddish-yellow network stretching from the nucleus to the periphery of the cell. A homogeneous, much less refractive substance lies in the meshes of the net. A similar, but coarser network is now seen in the shrunken nucleus. Sometimes this condition of the cells persists for a few seconds or minutes, or even hours or days, but more frequently, in the majority of cells, the observer is startled to see the entire body suddenly and symmetrically enlarge; the meshes of the new-formed network within the body spread out, the fibres becoming more slender, and often breaking away from the sides of the cell, and the whole becomes decolorized. The nucleus meanwhile may remain unchanged, looking however more distinct by contrast, or it may become shrunken, nearly homogeneous, and very strongly refractive. Sometimes upon the sudden enlargement of the cell the network in the body becomes so delicate as to be almost invisible, and it may altogether disappear.

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[1] I wish to correct an error which I committed in the paper above referred to, in calling the species of frog experimented upon with carbolic acid Rana esculenta : it was R. clamitans; the European species, R. esculenta, as I have been subsequently informed, not occurring in this country. This is a matter of no little importance, because, as is well known, there are considerable anatomical differences between different species of frogs, and also, as I have frequently observed, physiological peculiarities, in their power of resisting deleterious agencies, and in their reaction towards drugs, so marked as to make their recognition imperative in experimental studies.

The cells after this enlargement are still flattened ovoids, and about one-fifth larger than before. In some cases the change occurs so rapidly that the intermediate changes in the process are lost sight of or do not occur, and the enlarged cells, with their sharply defined nuclei and almost (sometimes quite) transparent colourless body, bounded by a delicate contour line, appear where but an instant before the eye of the observer was fixed upon a slightly mottled cell. Numerous slight departures from the above description may be observed, depending upon the directness with which the acid comes in contact with the cells, etc., but it is not necessary to describe them in detail here.

The network in the cell body, when its development is evident, may be readily stained with eosin and other colouring agents. It would seem most probable that its development is the result of the rapid disintegration of the protoplasm of the cell, perhaps a residuum of the stroma after the decomposition, or separation and discharge of the hæmoglobin, and not that it is a pre-formed structure analogous to the intracellular networks so freely described by certain authors. Somewhat similar appearances are produced in the cell by carbolic acid and other agents.

Strong Solutions on Mammalian Blood.—The action of salicylic acid, 1–500, upon the white blood-cells of the rabbit and of man is similar to that on the leucocytes of the frog, but the changes in the red cells are not as prominent as in those of the frog. There is at first the same mottling the cell and the formation of coarse, irregular, strongly refractive linear structures in or upon the cell, and then in almost all cases comes a sudden expansion and decoloration, and there is finally left a pale delicate spheroidal body which remains for a long time unchanged in the acid. Much less frequently at the instant that the agent touches the red cells, they enlarge and become globular, and the entire central portion is broken up into larger and smaller, often angular, strongly refractive particles which seem to float in a fluid within the unbroken contour of the cell. These little bodies immediately commence to dance to and fro within the cell, and at the same time to grow smaller; they rapidly decrease in size, dancing faster and faster as they do so until they entirely disappear, leaving a pale spheroidal body similar to the red cells after the action of water. Sometimes, before the particles within have disappeared, they are suddenly shot out of one side of the cell in a brush-like cluster, and immediately disappear in the surrounding fluid. The movements in the new formed particles resemble the Brownonian movements.

Dilute Solutions on Frog's Blood.—With solutions of the strength of 1–1000 to 1–4000, death of both kinds of cells occurs sooner or later, but without as marked, though similar, morphological changes in the protoplasm, as those produced by stronger solutions. In solutions of 1–4000 amœboid movements in the leucocytes may continue on the slide, with suitable precautions against concentration of the irrigating fluid, for several hours, but they are very slow from the first, and when they have once ceased cannot be reinstated by washing out with the indifferent salt solution, but the cells on the contrary rapidly disintegrate. The red blood-cells are affected by these dilute solutions apparently in the same way as by other dilute acids,[1] as acetic and hydrochloric, becoming at first slightly granular and then, often with a sudden jerk, swelling out and becoming decolorized, with shrinkage of the nucleus, and sometimes with the development of an irregular delicate fragmentary network within the cell-body.

Dilute Solutions on Mammalian Blood.—Solutions of 1–1000 to 1–4000 cause immediate cessation of amœboid movement in the leucocytes of man and the rabbit, when studied on the warm stage, and the nucleus soon becomes visible and the cell-body shrunken and coarsely granular. On the red blood-cells the effect is similar to that caused by other dilute acids; they rapidly swell, assuming a globular shape and become decolorized.

Action on the Circulation and Emigration.—This was studied in the bladder and mesentery of the living curārized frog; Thoma's frog-plate being used as in the former experiments.[2] The effects of solutions of varying strengths may be briefly summarized. Solutions of 1–500, and stronger, cause cloudiness of the tissue and a granular precipitate in the blood-serum; then permanent stasis occurs in all but the larger trunks, and usually in these too after a few moments. The arteries and veins may contract slightly at first, but they then dilate largely (especially the veins) as stasis occurs, and very soon the blood-cells within undergo the same changes as when they are treated with the acid on the slide.

With more dilute solutions, 1–1000 to 1–3000, stasis comes on less promptly, but very surely within a few minutes or hours, and is accompanied or followed by the same morphological changes in the blood-cells as are produced outside of the vessels. With still more dilute solutions, 1–4000, the circulation may continue in vigorous animals for many hours, twenty-four to thirty-six and over,[1] with but slight cloudiness of the tissues, and no evident changes in the bloodvessels beyond the usual inflammatory dilatation; *but emigration either does not occur at all or only to a very slight extent.* The parietal fixture of the leucocytes, which occurs under simple salt solution, is but slightly marked or almost entirely absent from the first, the cells rolling along as usual in the peripheral zone, but remaining spheroidal, and exhibiting little tendency to stick and drag along the walls. If the part is at first irrigated with salt solution until emigration is well established and this is then replaced by the salicylic solution, emigration very soon ceases and the parietal fixture of the cells becomes less marked, while the cells which have already passed out and are free in the tissues soon cease their perigrinations. In no case was it found possible to cause a re-establishment of emigration after it had once been stopped by the acid; a difference between the action of salicylic and carbolic acid which would seem to be of considerable significance.

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[1] Kneuttinger, Zur Histologie des Blutes, Würzburg, 1865, p. 28. Stirling, Text-book of Practical Histology, 1881, p. 2.

[2] l. c., p. 86.

SUMMARY—*Frog.*—Salicylic acid in very dilute solutions, 1–4000, checks or entirely suppresses emigration of white blood-cells in the bladder and mesentery, without sensibly affecting the calibre of the bloodvessels or the general character of the circulation, or the structure of the blood-cells. It also retards amœboid movements both in the tissues and upon the slide. Somewhat stronger solutions, 1–1000, cause stasis in the bloodvessels, death of the white blood-cells, and swelling and decoloration of the red cells in a manner similar to other dilute acids. Solutions of 1–500 cause instantaneous stasis; death of the leucocytes with disintegration of the protoplasm; while in the red cells it produces immediate decomposition of the protoplasm with decoloration and a separation into morphologically distinct elements, which may remain permanent in the acid, or undergo subsequent changes.

Man and Rabbit.—Dilute solutions, 1–1000 to 1–4000, cause cessation of amœboid movement in the leucocytes, with death of the cell and disintegration of the protoplasm, and in the red cells swelling and decoloration. Strong solutions, 1–500, cause instantaneous death of both kinds of cells, with marked morphological degenerative changes.

Remarks.—It will be seen by a comparison of the above results with those obtained in the experiments on carbolic acid that the latter is less inimical, in solutions of the same percentage strength, to the life and functions of the blood-cells than is salicylic acid. For neither upon the slide nor in the bloodvessels or the tissues can the movement of the leucocytes be re-established when they have been brought to rest by salicylic acid, and the morphological changes produced by it are much more prompt and marked. It does not of course follow from these experiments that the action of salicylic acid in restraining emigration is peculiar to it in virtue of any properties other than those which it possesses in common with such dilute acids as acetic and hydrochloric, for these also in dilute solution are capable of restraining emigration, although with the exhibition of somewhat different phenomena. It is sufficient for the purposes of this paper to have shown experimentally, *that salicylic acid does restrain emigration, and is inimical in strong solutions to the life, and in dilute solutions to the activity of the white blood-cells;* and to suggest, as was done in the case of carbolic acid, the probability that some of its favourable effects, when applied as a surgical dressing, are due to its direct action upon the living white blood-cells.

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[1] It should be remembered that emigration often commences in the bladder within a very short time after exposure of the part, sometimes within an hour.

Literature.—Closely upon Kolbe's announcement, in 1874, of a new method by which salicylic acid could be prepared cheaply and in large quantities, followed a flood of literature which has continued with little abatement to the present time. But among the hosts of valuable papers little is found in regard to the direct action of this agent upon the blood-cells, or locally upon the circulation.

Cotton[1] studied the effects produced by it on blood in the mass, with the view of determining the differences in its action upon the blood of different mammals, for medico-legal purposes. He notes that with three per cent. solutions the red cells become globular, and that the hæmoglobin is decomposed with formation of hæmatin. He also states that one per cent. solutions cause the central portion of the leucocytes to become more transparent, and gives them a double contour, from which he infers that these cells are furnished with a double membrane.

Thiersch[2] states, without giving the details of his experiments, that as a result of its action the central portion of the red cells becomes transparent, while a sharply defined peripheral zone remains deep yellow; and further that this peripheral ring may separate from the central portion and break up, at regular intervals, into segments, which form little free chains in the fluid. Under the conditions of his experiments the writer did not notice such appearances.

Béchamp,[3] who studied the action of salicylic acid upon the lower vegetable organisms, yeast, etc., found that dilute solutions, while sometimes modifying their structure, did not necessarily kill them, but did suspend their functional activity. These experiments, so far as the writer has the literature at command, are all that bear directly upon the theme of the present study. Of the numerous experiments upon its action on the lower organisms, those of Béchamp are mentioned in this connection only as showing an inhibitory action of salicylic acid upon the function of vegetable organisms apparently analogous to that above recorded upon animal cells.

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[1] Cotton, Action de l'acide salicylique sur le sang et en particulier sur les globules, Lyon, Méd. 50, p. 557, 1877.

[2] Thiersch, Volkmann's Klinische Vorträge, Nos. 84 and 85, p. 657.

[3] Béchamp, Observations sur les antiseptiques, Montpelier Med., Janv. p. 30, Fev. p. 134, 1876.

ARTICLE IV.

THE SMALL PUSTULAR SCROFULODERM.[1] By LOUIS A. DUHRING, M.D.,

Professor of Skin Diseases in the Hospital of the University of Pennsylvania.

FROM time to time I have met with instances of a rare and striking form of skin disease, to which I desire to call the attention of this Association. There are several reasons why the subject is worthy of investigation. In the first place, the disease is unquestionably rare. Up to the present time but three or four cases have come to my notice. Secondly, the process is characterized by marked and well-defined lesions, and tends to pursue an obstinate and chronic course. It, moreover, always terminates in scarring. Thirdly, the disease is liable to be mistaken for other processes, especially for the small pustular syphiloderm, which it very closely resembles. I have already described the general features of the disease briefly in the second edition of my "Treatise on Diseases of the Skin," page 454, under Scrofuloderma, where it seemed to me it might, for the present, be placed. The account I have given of it in my treatise is as follows:—

"Another variety of disease, of which I have never seen any account in literature, and which, I think, must be viewed as a manifestation of scrofulosis, consists in the formation of pin-head and small split-pea sized, disseminated, yellowish, flat pustules, with usually a raised violaceous areola. In general appearance the lesions resemble those of the small pustular syphiloderm. They crust over gradually in the course of from one to several weeks, with depressed, shrunken, hard or horny, yellowish or grayish, adherent crusts, which in time drop off, leaving marked, punched-out looking, indelible scars, resembling those of variola. The lesions are further characterized by a sluggish, chronic course, and may last weeks or months. They appear at irregular periods, new ones coming out as the older ones disappear, so that the patient is rarely free of them. The disease may continue for years. It may occur upon any region, but in the cases that I have encountered has shown a disposition to appear about the

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[1] Read at the fifth annual meeting of the American Dermatological Association, Newport, R. I., Aug. 31, 1881.